



PTO/SB/21 (09-04)

Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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DAC
JFW

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

21

Application Number

10/575,991

Filing Date

April 13, 2006

First Named Inventor

Lital Alfonta

Group Art Unit

1656

Examiner Name

Kagnew H. Gebreyesus

Attorney Docket Number

54-000711US

ENCLOSURES (check all that apply)

- ☐ Fee Transmittal Form
☐ Fee Attached
☐ Amendment / Response
☐ Amendment and Request for Reconsideration
☐ Affidavits/declaration(s)
☐ Extension of Time Request
☒ Receipt Acknowledgement Postcard
☐ Information Disclosure Statement
☐ Certified Copy of Priority Document(s)
☐ Response to Missing Parts/ Incomplete Application
☐ Response to Missing Parts under 37 CFR 1.52 or 1.53

- ☐ PTO-1449 Form
☐ Cited References
☐ Copy of PCT Search Report
☐ Copy of EP Search Report
☐ Petition to Convert to a Provisional Application
☐ Power of Attorney, Revocation Change of Correspondence Address
☐ Terminal Disclaimer
☐ Small Entity Statement
☐ Request for Refund

- ☒ Petition to Withdraw Holding of Abandonment
☒ Copy of Receipt Acknowledgement Postcard stamped by USPTO
☒ Copy of Response Submitted 09/26/2007
☒ Copy of 1st page of Response from PAIRS
☐ Status Letter
☐ Additional Enclosure(s) (please identify below):

Authorization to Charge Deposit Account

Please charge Deposit Account No. 50-0893 for any additional fees associated with this paper or during the pendency of this application, including any extensions of time for consideration of the documents enclosed.

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENTFirm
or
Individual name

Jonathan Alan Quine, Reg. No. 41,261, Quine Intellectual Property Law Group, P.C.

Signature

Date

October 17, 2007

CERTIFICATE OF MAILING

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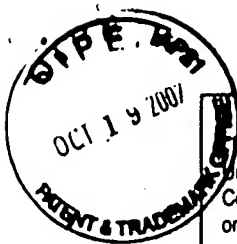
Typed or printed name

Deborah Berwick

Signature

Date

October 17, 2007



CERTIFICATE OF MAILING	
I hereby certify that this correspondence is being deposited with the United States Postal Service first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on <u>October 17, 2007</u> .	
QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.	
By: <u>Deborah Berwick</u>	
Deborah Berwick	

Appl. No.	:	10/575,991	Confirmation No. 2082
Applicant	:	Lital Alfonta, et al.	
Filed	:	April 13, 2006	
TC/A.U.	:	1656	
Examiner	:	Kagnew H. Gebreyesus	
Docket No.	:	54-000711US	
Customer No.	:	22798	
Client Ref No.:	:	1009.1 US / NOV0608P	
Novartis Ref. No.:	:	DC/4-33965/SCR	

Mail Stop Petitions
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

**PETITION TO WITHDRAW HOLDING OF ABANDONMENT WITH
CONTINGENT PETITION TO REVIVE UNINTENTIONALLY ABANDONED
APPLICATION**

PETITION TO WITHDRAWN HOLDING OF ABANDONMENT

Applicants request withdrawal of the clearly erroneous Notice of Abandonment received in the above case. The facts are as follows.

(1) Applicants received a first office action on the merits on March 26, 2007, setting a three month date for response, extendible to six months using the usual provisions of 37 C.F.R. 1.136(a).

(2) Applicants **timely filed** a "RESPONSE TO FIRST OFFICE ACTION, AMENDMENT AND REQUEST FOR RECONSIDERATION" on September 26, 2007, with a three month petition to extend the period for response through the filing date of the response. A copy of Applicants' submission, marked "copy" is provided herewith. Proper

certificate of mailing procedures were used throughout the submission to indicate that the submission was timely deposited with the US Post Office on September 26, 2007, thus setting the filing date for the submission, pursuant to 37 C.F.R. § 1.8.

(3) Applicants received a stamped post card from OIPE, plainly indicating that the Patent Office received Applicants submission (date stamped postcard showing date of receipt of September 28), *copy enclosed*. The date of receipt stamped by the USPTO is entirely consistent with Applicants' date of mailing, further evidencing that Applicants' timely mailed the response.

(4) Applicants response appears on the USPTO PAIRS system as of the date of this petition, with a receipt date of September 28, 2007, further unequivocally demonstrating that the Patent Office received Applicants' timely submission. A copy of the first page, with the date received stamp, is printed from PAIRS and provided herewith.

(5) Applicants' Attorney's deposit account was charged both for the fees associated with the filing of the amendment (on October 1, 2007) and for excess claim fees associated with the amendment (on October 5, 2007), further plainly indicating that the Office received Applicants' timely submission, and also plainly indicating a more than sufficient balance in the deposit account to cover any fees associated with the submission.

(6) Despite the above, Applicants received an ERRONEOUS Notice of Abandonment on October 15, 2007, incorrectly alleging failure to provide a response to the Office Action of March 26, 2007. The mail date on the Notice was October 9, 2007.

Clearly, the Office has made an error in the subject Notice of Abandonment. A response to the first Action on the merits (March 26, 2007) was plainly made, as demonstrated by the stamped return receipt post card, appearance of the amendment in PAIRS and the charge to Applicants' deposit account for fees associated with the response. Accordingly, **THE NOTICE OF ABANDONMENT MUST IMMEDIATELY BE WITHDRAWN.**

Further, Applicants must be granted a patent term adjustment to extend the period of patent term on any case that arises out of the instant application to account for the complete period between the ERRONEOUS Notice of Abandonment, and a proper

withdrawal of the holding of abandonment. Finally, because the Notice of Abandonment was a clear error, the Office should expedite consideration of this petition.

In the event that the petition to withdrawn the holding of abandonment is not granted, Applicants formally request a teleconference with the Officer deciding this petition and an appropriate supervisor.

CONTINGENT PETITION TO REVIVE

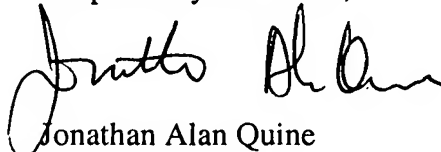
Solely in the event that the above petition to withdraw the holding of abandonment is NOT granted, Applicants petition to revive the application for unintentional abandonment. Applicants note that they strongly dispute any alleged abandonment for the reasons noted above. Applicants timely filed an appropriate response, and the Office's Notice of Abandonment was clear error.

In light of the above, Applicants note that any purported abandonment was also at least unintentional. Applicants hereby state that the entire delay was unintentional. Please charge Applicants any fees that may be associated with this petition to revive.

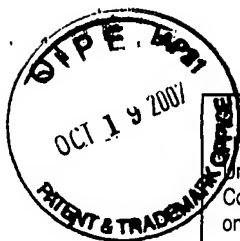
Applicants note that the requisites of a petition to revive (MPEP 711.03(c)) are clearly provided herewith, i.e., a statement that the entire delay was unintentional, an appropriate reply (in the form of the copy of the RESPONSE TO FIRST OFFICE ACTION, AMENDMENT AND REQUEST FOR RECONSIDERATION provided herewith), and authorization to charge fees for the petition. **Solely in the event that the above petition to withdraw is not granted, please revive the application pursuant to this contingent petition.**

QUINE INTELLECTUAL PROPERTY LAW GROUP
P.O. BOX 458, Alameda, CA 94501
Tel: 510 337-7871
Fax: 510 337-7877
PTO Customer No.: **22798**
Deposit Account No.: **50-0893**
Attachments:

Respectfully submitted,


Jonathan Alan Quine
Reg. No: 41,261

- 1) A transmittal sheet;
- 2) Copy of Receipt Acknowledgement Postcard stamped by USPTO;
- 3) Copy of Response Submitted September 26, 2007;
- 4) Copy of 1st page of Response from PAIRS; and,
- 5) A receipt indication postcard.



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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.

By: Deborah Berwick
Deborah Berwick

Appl. No.	:	10/575,991	Confirmation No. 2082
Applicant	:	Lital Alfonta, et al.	
Filed	:	April 13, 2006	
TC/A.U.	:	1656	
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CONTINGENT PETITION TO REVIVE

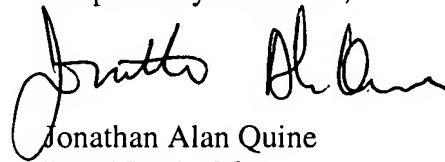
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P.O. BOX 458, Alameda, CA 94501
Tel: 510 337-7871
Fax: 510 337-7877
PTO Customer No.: **22798**
Deposit Account No.: **50-0893**
Attachments:

Respectfully submitted,


Jonathan Alan Quine
Reg. No: 41,261

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- 2) Copy of Receipt Acknowledgement Postcard stamped by USPTO;
- 3) Copy of Response Submitted September 26, 2007;
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- 5) A receipt indication postcard.



COPY

RECEIVED

OCT 05 2007

Quine Intellectual Property Law Group, P.C.

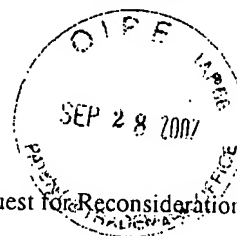
TO THE U.S. PATENT & TRADEMARK OFFICE

Please stamp the date of receipt of the following document(s) and return this card to us

RE: Response to Office Action, Amendment and Request for Reconsideration for
SITE-SPECIFIC INCORPORATION OF REDOX ACTIVE AMINO ACIDS INTO
PROTEINS

TITLE OF DOCUMENT(S):

- Transmittal
- Fee Transmittal
- Response to Office Action, Amendment and Request for Reconsideration (12 pages)
- Request for extension of time
- Receipt Acknowledgement Postcard



Application No. 10/575,991

File No. 54-000711US

Date Due June 26, 2007

Date Mailed September 26, 2007

Atty/Secty. EJD/kc



COPY

PTO/SB/21 (09-04)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/575,991		
	Filing Date	April 13, 2006	
	First Named Inventor	Lital Alfonta	
	Group Art Unit	1656	
	Examiner Name	Kagnew H. Gebreyesus	
Total Number of Pages in This Submission		Attorney Docket Number	54-000711US

ENCLOSURES (check all that apply)

<input checked="" type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> PTO-1449 Form	<input type="checkbox"/> Interview Summary
<input type="checkbox"/> Fee Attached	<input type="checkbox"/> Cited References	<input type="checkbox"/> Request for Continued Examination (RCE)
<input checked="" type="checkbox"/> Amendment / Response	<input type="checkbox"/> Copy of PCT Search Report	<input type="checkbox"/> Request for Corrected Filing receipt
<input checked="" type="checkbox"/> Response to Office Action, Amendment and Request for Reconsideration	<input type="checkbox"/> Copy of EP Search Report	<input type="checkbox"/> Copy of Filing Receipt - marked up
<input type="checkbox"/> Affidavits/declaration(s)	<input type="checkbox"/> Petition to Convert to a Provisional Application	<input type="checkbox"/> Status Letter
<input checked="" type="checkbox"/> Extension of Time Request	<input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address	<input type="checkbox"/> Additional Enclosure(s) (please identify below):
<input checked="" type="checkbox"/> Receipt Acknowledgement Postcard	<input type="checkbox"/> Terminal Disclaimer	
<input type="checkbox"/> Information Disclosure Statement	<input type="checkbox"/> Small Entity Statement	
<input type="checkbox"/> Certified Copy of Priority Document(s)	<input type="checkbox"/> Request for Refund	
<input type="checkbox"/> Response to Missing Parts/ Incomplete Application	Authorization to Charge Deposit Account Please charge Deposit Account No. 50-0893 for any additional fees associated with this paper or during the pendency of this application, including any extensions of time for consideration of the documents enclosed.	
<input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	Remarks	

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Edward J. DesJardins, Ph.D., Reg. No. 51,162, Quine Intellectual Property Law Group, P.C.
Signature	
Date	September 26, 2007

CERTIFICATE OF MAILING

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Typed or printed name	Kimberly Cheung		
Signature		Date	September 26, 2007

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PTO/SB/17 (12-04v2)

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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OCT 19 2007

Effective on 12/08/2004.

Form pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).

FEE TRANSMITTAL
For FY 2005

Complete if Known

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT (\$)

1020.00

Application Number

10/575,991

Filing Date

April 13, 2006

First Named Inventor

Lital Alfonta

Examiner Name

Kagnew H. Gebreyesus

Art Unit

1656

Attorney Docket No.

54-000711US

METHOD OF PAYMENT (check all that apply)

☐ Check ☐ Credit Card ☐ Money Order ☐ None ☒ Other (please identify): Deposit Account

☒ Deposit Account Deposit Account Number: 50-0893 Deposit Account Name: Quine Intellectual Property Law Group, P.C.

For the above identified deposit account, the Director is hereby authorized to: (check all that apply)

☒ Charge fee(s) indicated below ☐ Charge fee(s) indicated below, except for the filing fee

☒ Charge any additional fee(s) or underpayments of fee(s) under 37 CFR 1.16 and 1.17 ☒ Credit any overpayments

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

Application Type	FILING FEES		SEARCH FEES		EXAMINATION FEES		Fees Paid (\$)
	Fee (\$)	Small Entity Fee (\$)	Fee (\$)	Small Entity Fee (\$)	Fee (\$)	Small Entity Fee (\$)	
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

2. EXCESS CLAIM FEES

Fee Description	Fee (\$)	Small Entity Fee (\$)
Each claim over 20 (Including Reissues)	50	25
Each independent claim over 3 (including Reissues)	200	100
Multiple dependent claims	360	180
Total Claims		
Extra Claims		
Fee (\$)		
Fee Paid (\$)		
- 20 or HP =	x	=
HP = highest number of total claims paid for, if greater than 20.		
Indep. Claims		
Extra Claims		
Fee (\$)		
Fee Paid (\$)		
- 3 or HP =	x	=
HP = highest number of independent claims paid for, if greater than 3.		

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 27 CFR 1.16(s).

Total Sheets Extra Sheets Number of each additional 50 or fraction thereof (\$) Fee Paid (\$)

- 100 /50 = Round up to a whole number) x =

4. OTHER FEE(S)

Non-English Specification, \$130 fee (no small entity discount)

Other (e.g., late filing surcharge):

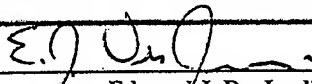
Other: Petition for 3-month Extension of Time

1020.00

Other: Other: Other: Other: Other:

SUBMITTED BY

Signature

Registration No.
(Attorney/Agent)

51,162

Telephone

(510) 337-7871

Name (Print/Type)

Edward J. DesJardins, Ph.D.

Date

September 26, 2007

COPY

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)

Docket Number (Optional)
54-000711US



In re Application of Lital Alfonta, et al.

Application Number: 10/575,991

Filed: April 13, 2006

For SITE-SPECIFIC INCORPORATION OF REDOX ACTIVE AMINO ACIDS INTO PROTEINS

Group Art Unit 1656

Examiner Kagnew H. Gebreyesus

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a response in the above-identified application.

The requested extension and appropriate non-small-entity fee are as follows
(check time period desired):

- | | | |
|-------------------------------------|---|--------|
| <input type="checkbox"/> | One month (37 CFR 1.17(a)(1)) | \$120 |
| <input type="checkbox"/> | Two months (37 CFR 1.17(a)(2)) | \$450 |
| <input checked="" type="checkbox"/> | Three months (37 CFR 1.17(a)(3)) | \$1020 |
| <input type="checkbox"/> | Four months (37 CFR 1.17(a)(4)) | \$1590 |
| <input type="checkbox"/> | Five months (37 CFR 1.17(a)(5)) | \$2160 |
| <input type="checkbox"/> | Applicant is a small entity under 37 CFR 1.9 and 1.27, therefore the fee amount shown above is reduced by one-half, and the resulting fee is: \$ _____. | |

A small entity statement under 37 CFR 1.27:

- ☐ is enclosed.
- ☐ has already been filed in this application.

- ☐ A check in the amount of the fee is enclosed.
- ☐ The Commissioner has already been authorized to charge fees in this application to a Deposit Account.
- ☒ The Commissioner is hereby authorized to charge any fees that may be required, or credit any overpayment, to Deposit Account Number 50-0893.

- I am the ☐ assignee of record of the entire interest.
- ☐ applicant.
- ☒ attorney or agent of record.
- ☐ attorney or agent under 37 CFR 1.34(a)
Registration number if acting under 37 CFR 1.34(a): _____

Sept. 26, 2007
Date

E. J. DesJardins
Signature

Edward J. DesJardins, Ph.D., 51,162
Typed or printed name and Reg. No.

CERTIFICATE OF MAILING

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Typed or
Printed Name

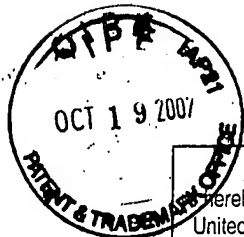
Kimberly Cheung

Signature

Kimberly Cheung

Date

September 26, 2007



COPY

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Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450,
on September 24, 2007

QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.

By: Kimberly Cheung
Kimberly Cheung

Appl. No. : 10/575,991
Applicant : Lital Alfonta, *et al.*
Filed : April 13, 2006
TC/Art Unit : 1656
Examiner : Kagnev H. Gebreyesus

Confirmation No. 2082

Docket No. : 54-000711US
Customer No. : 22798
Client Ref No.: 1009.1 US / NOV0608P
Novartis Ref. No. DC/4-33965/SCR

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**RESPONSE TO FIRST OFFICE ACTION, AMENDMENT and REQUEST FOR
RECONSIDERATION**

Sir:

In response to the Office Action dated March 26, 2007, please amend the above-identified application as indicated herein. Please reconsider the application in light of the amendments and remarks below.

Amendment to the Claims is reflected in the listing of claims that begins on page 2 of this paper.

Remarks/Arguments begin on page 8 of this paper.

AMENDMENT TO THE CLAIMS

Please amend the claims as shown below. This listing of claims will replace all prior versions and listings of claims in the application. Deletions of text are indicated with ~~strikethrough~~ or double bracket ~~[[x]]~~. Added text is shown by underline.

LISTING OF THE CLAIMS:

1. **(withdrawn)** A composition comprising an orthogonal aminoacyl-tRNA synthetase (O-RS), wherein the O-RS preferentially aminoacylates an O-tRNA with a redox active amino acid.
2. **(withdrawn)** The composition of claim 1, wherein the O-RS comprises an amino acid sequence comprising SEQ ID NO.: 1, or a conservative variation thereof.
3. **(withdrawn)** The composition of claim 1, wherein the O-RS preferentially aminoacylates the O-tRNA with an efficiency of at least 50% of the efficiency of a polypeptide comprising an amino acid sequence of SEQ ID NO.: 1.
4. **(withdrawn)** The composition of claim 1, wherein the O-RS is derived from a *Methanococcus jannaschii*.
5. **(withdrawn)** The composition of claim 1, comprising a cell.
6. **(withdrawn)** The composition of claim 5, wherein the cell is an E. coli cell.
7. **(withdrawn)** The composition of claim 1, comprising a translation system.
8. **(withdrawn)** A cell comprising a translation system, wherein the translation system comprises:
 - an orthogonal -tRNA (O-tRNA);
 - an orthogonal aminoacyl-tRNA synthetase (O-RS); and,
 - a redox active amino acid;
 - wherein the O-tRNA recognizes a first selector codon, and the O-RS preferentially aminoacylates the O-tRNA with the first redox active amino acid.

9. (withdrawn) The cell of claim 8, wherein the O-RS preferentially aminoacylates the O-tRNA with an efficiency of at least 50% of the efficiency of a polypeptide comprising an amino acid sequence of SEQ ID NO.: 1.
10. (withdrawn) The cell of claim 8, wherein the O-tRNA comprises or is encoded by a polynucleotide sequence as set forth in SEQ ID NO.: 2, or a complementary polynucleotide sequence thereof, and wherein the O-RS comprises an amino acid sequence comprising SEQ ID NO.: 1, or a conservative variation thereof.
11. (withdrawn) The cell of claim 8, wherein the cell further comprises an additional different O-tRNA/O-RS pair and unnatural amino acid, wherein the O-tRNA recognizes a second selector codon and the O-RS preferentially aminoacylates the O-tRNA with the second unnatural amino acid.
12. (withdrawn) The cell of claim 8, wherein the cell is a non-eukaryotic cell.
13. (withdrawn) The cell of claim 12, wherein the non-eukaryotic cell is an *E. coli* cell.
14. (withdrawn) The cell of claim 8, further comprising a nucleic acid that comprises a polynucleotide that encodes a polypeptide of interest, wherein the polynucleotide comprises a selector codon that is recognized by the O-tRNA.
15. (withdrawn) An *E. coli* cell, comprising:
 - an orthogonal tRNA (O-tRNA);
 - an orthogonal aminoacyl- tRNA synthetase (O-RS), wherein the O-RS preferentially aminoacylates the O-tRNA with a redox active amino acid;
 - the redox active amino acid; and,
 - a nucleic acid that encodes a polypeptide of interest, wherein the nucleic acid comprises the selector codon that is recognized by the O-tRNA.
16. (withdrawn) The *E. coli* cell of claim 15, wherein the O-RS preferentially aminoacylates the O-tRNA with an efficiency of at least 50% of the efficiency of a polypeptide comprising an amino acid sequence of SEQ ID NO.: 1.
17. (withdrawn) An artificial polypeptide comprising SEQ ID NO. 1.
18. (withdrawn) An artificial polynucleotide that encodes a polypeptide of claim 17.

19. (withdrawn) A vector comprising or encoding a polynucleotide of claim 18.
20. (withdrawn) The vector of claim 19, wherein the vector comprises a plasmid, a cosmid, a phage, or a virus.
21. (withdrawn) The vector of claim 19, wherein the vector is an expression vector.
22. (withdrawn) A cell comprising the vector of claim 19.
23. (withdrawn) A method for identifying an orthogonal-aminoacyl-tRNA synthetase for use with an O-tRNA that utilizes a redox amino acid, the method comprising:
 - subjecting to selection a population of cells of a first species, wherein the cells each comprise:
 - 1) a member of a plurality of aminoacyl-tRNA synthetases (RSs);
 - 2) the orthogonal tRNA (O-tRNA) derived from one or more species; and,
 - 3) a polynucleotide that encodes a selection marker and comprises at least one selector codon;wherein cells that are enhanced in suppression efficiency as compared to cells lacking or comprising a reduced amount of the member of the plurality of RSs that comprises an active RS that aminoacylates the O-tRNA; and,
 - selecting the active RS that aminoacylates the O-tRNA with the redox active amino acid, thereby providing the orthogonal -aminoacyl-tRNA synthetase for use with the O-tRNA.
24. (withdrawn) The method of claim 23, wherein the selection comprises a positive selection and the selection marker comprises a positive selection marker.
25. (withdrawn) The method of claim 23, wherein the plurality of RSs comprise mutant RSs, RSs derived from one or more species other than the first species or both mutant RSs and RSs derived from a species other than the first species.
26. (withdrawn) An orthogonal aminoacyl-tRNA synthetase identified by the method of claim 23.

27. (withdrawn) A method of producing a protein in a cell with a redox active amino acid at a specified position, the method comprising:

a) growing, in an appropriate medium, the cell, where the cell comprises a nucleic acid that comprises at least one selector codon and encodes a protein; and,

b) providing the redox active amino acid;

wherein the cell further comprises:

an orthogonal -tRNA (O-tRNA) that functions in the cell and recognizes the selector codon; and,

an orthogonal aminoacyl-tRNA synthetase (O-RS) that preferentially aminoacylates the O-tRNA with the redox active amino acid, wherein said O-RS:

i) has an efficiency that is at least 50% of the efficiency observed for a translation system comprising said O-tRNA, said redox active amino acid, and an aminoacyl-tRNA synthetase comprising the amino acid sequence of SEQ ID NO: 1; or

ii) preferentially aminoacylates said O-tRNA with a redox active amino acid selected from the group consisting of a 3,4-dihydroxy-L-phenylalanine (DHP), a 3,4,5-trihydroxy-L-phenylalanine, a 3-nitro-tyrosine, a 4-nitro-phenylalanine and a 3-thiol-tyrosine; and

c) incorporating the redox active amino acid into the specified position in the protein during translation of the nucleic acid with the at least one selector codon, thereby producing the protein with a redox active amino acid at a specified position.

28. (withdrawn) The method of claim 27, wherein the O-RS comprises an amino acid sequence which comprises SEQ ID NO.: 1.

29. (withdrawn) The method of claim 27, wherein the cell is a non-eukaryotic cell.

30. (withdrawn) The method of claim 29, wherein the non-eukaryotic cell is an *E. coli* cell.

31. (currently amended) A composition comprising a protein, wherein the protein comprises two or more [[a]] redox active amino acids ~~acid~~ selected from the group consisting

of: a 3,4-dihydroxy-L-phenylalanine (DHP), a 3,4,5-trihydroxy-L-phenylalanine, a 3-nitro-tyrosine, a 4-nitro-phenylalanine, and a 3-thiol-tyrosine.

32. (cancelled)

33. (original) The composition of claim 31, wherein the protein comprises an amino acid sequence that is at least 75% identical to that of a wild-type therapeutic protein, a diagnostic protein, an industrial enzyme, or portion thereof.

34. (original) The composition of claim 31, wherein the composition comprises a pharmaceutically acceptable carrier.

35. (currently amended) The composition of claim 31, wherein the protein further comprises at least one two or more unnatural amino acid acids that is not a 3,4-dihydroxy-L-phenylalanine (DHP), a 3,4,5-trihydroxy-L-phenylalanine, a 3-nitro-tyrosine, a 4-nitro-phenylalanine, or a 3-thiol-tyrosine.

36. (currently amended) The composition of claim 31, wherein the protein comprises two or more redox active unnatural amino acids that ~~, wherein two or more of said unnatural amino acids are the same.~~

37. (cancelled)

38. (currently amended) The composition of claim 31, wherein at least the protein ~~comprises two or more unnatural~~ of said redox active amino acids that are different.

39. (previously presented) The composition of claim 31, wherein the protein comprises a myoglobin polypeptide or a portion thereof.

40. (cancelled)

41. (previously presented) The composition of claim 31, wherein the protein is capable of undergoing oxidation.

42. (currently amended) The composition of claim 31, wherein the protein is capable of undergoing (i) oxidation or (ii) a shift in reductive peak potential as measured by voltammetric response in comparison to a corresponding protein that lacks said at least two redox active amino acids improved oxidation, and wherein said oxidation or shift in reductive

peak potential require improved oxidation requires said at least two redox active amino acids
acid.

43. (currently amended) The composition of claim 31, wherein at least one the of said
two or more redox active amino acids acid is 3,4-dihydroxy-L-phenylalanine (DHP).

44. (previously presented) The composition of claim 31, wherein the redox active
amino acid is a redox catalyst.

45. (new) The composition of claim 31, further comprising:

- i) at least one orthogonal tRNA (O-tRNA);
- ii) at least one orthogonal aminoacyl- tRNA synthetase (O-RS), wherein the O-RS
preferentially aminoacylates the O-tRNA with at least one of said redox active
amino acids; and
- iii) a nucleic acid that encodes the protein, wherein the nucleic acid comprises at least
two selector codons that are recognized by the O-tRNA.

46. (new) The composition of claim 31, further comprising an O-RS comprising an
amino acid sequence comprising SEQ ID NO.: 1, or a conservative variant thereof.

47. (new) The composition of claim 31, further comprising an O-RS that has an
efficiency in a translation system that is at least 50% of the efficiency observed in a
translation system comprising an O-tRNA, an aminoacyl-tRNA synthetase comprising the
amino acid sequence of SEQ ID NO: 1 that preferentially aminoacylates the O-tRNA with at
least one of said redox active amino acids, and a nucleic acid encoding a polypeptide of
interest, said nucleic acid comprising at least one selector codon that is recognized by the O-
tRNA.

REMARKS/ARGUMENTS

Applicants provide herewith an amendment to the claims as described above.

Support for the amendment to the claims is found in the specification as originally filed, and is further discussed below. Applicants submit that no new matter has been added by way of the above Amendment. Accordingly, entry of the Amendment is respectfully requested.

The Office Action dated March 26, 2007, included claim objections and rejections based on alleged indefiniteness (35 U.S.C. §112, second paragraph) and alleged anticipation (35 U.S.C. §102). Applicants traverse all rejections to the extent that they may be applied to the amended claims, for the reasons noted herein. The present Response with Amendment is fully responsive to each of the Examiner's points, and Applicants respectfully request reconsideration of the claims in view of the amendments and remarks herein.

THE STATUS OF THE CLAIMS

Following entry of the present amendment, Claims 1-31, 33-35, 37-39, 41-44 and new claims 45-47 are pending. Claims 31, 35, 36, 38, 38, 42 and 43 are amended herein. Claims 32, 37 and 40 are cancelled. This amendment to the claims introduces no new matter. These amendments are made without prejudice and are not to be construed as abandonment of any originally claimed subject matter or presently claimed subject matter or agreement with any objection or rejection of record.

Support for new claims 45-47 is found throughout the specification. For example:

Claim Number	Location of Support in the Specification
45	Throughout the specification, and see specifically paragraphs 0009 and 0056.
46	See paragraphs 0006, 0012 and 0077.
47	See paragraphs 0006, 0009 and 0114.

CLAIM OBJECTIONS

The Examiner objected to claim 40 as allegedly being of improper dependent form. Solely for the purpose of advancing the prosecution of the present application, Applicants

have cancelled claim 40 in the present amendment, thereby rendering the objection moot. Applicants respectfully request withdrawal of the objection.

35 U.S.C. § 112, SECOND PARAGRAPH

In the Office Action, the Examiner rejected claim 33 under 35 U.S.C. § 112, second paragraph as indefinite. The Examiner states that the limitation "at least 75% identical to that of a wild-type therapeutic protein, a diagnostic protein, an industrial enzyme, or portion thereof" allegedly lacks proper antecedent basis because no sequences are provided in the application.

Applicants respectfully disagree, and traverse the rejection. The specification provides non-exhaustive lists of useful therapeutic and diagnostic proteins and industrial enzymes that can be modified to comprise two or more redox active amino acids (see paragraphs 0170, 0172 and 0173). No attempt is made to provide all sequences or even identify all known proteins that can be modified to contain redox active amino acids. DNA and protein sequence repositories are widely known in the art and are readily obtainable, for example as taught in the specification, from GenBank, EMBL, DDBJ and the NCBI (see paragraphs 0169 and 0174). One of ordinary skill in the art readily recognizes that GenBank keyword searches on the National Center for Biotechnology Information (NCBI) BLAST website or searches of the published scientific literature using NCBI PubMed will readily reveal the nucleotide and amino acid sequences of countless genes of medical and industrial value. Providing the sequences of these proteins in the specification is not necessary to meet the requirements of 35 U.S.C. § 112, second paragraph because it is understood that the sequences referred to in claim 33 can be readily obtained from public sources (as taught in the specification). Applicants respectfully request withdrawal of the rejection.

In the Office Action, the Examiner rejected claim 42 under 35 U.S.C. § 112, second paragraph as indefinite for an alleged lack of clarity for the expression "improved oxidation." Applicants respectfully disagree, and traverse the rejection.

Regardless, solely for the purpose of advancing the prosecution of the present application, and without acquiescing to the Examiner's rejection, the Applicants have amended claim 42. Rebuttal to the Examiner's rejection is made in view of the amended form of claim 42. Amended claim 42 replaces the expression "improved oxidation" with the

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expression "shift in reductive peak potential as measured by voltammetric response in comparison to a corresponding protein that lacks said at least two redox active amino acids." Clear support for this language is found at paragraph 0188. Use of this language removes any ambiguity that may have existed in the originally filed version of the claim. In view of amended claim 42, Applicants respectfully request withdrawal of the rejection.

35 U.S.C. §102

Alfonta *et al.* is Not Prior Art

In the Office Action, the Examiner rejected claims 31, 33, 34 and 39-44 under 35 U.S.C. §102(a) as allegedly anticipated by (or obvious over) Alfonta *et al.* "Site Specific Incorporation of a Redox-Active Amino Acid into Proteins," *Journal of the American Chemical Society* 125:14662-14663 (published November 6, 2003).

It appears that the Examiner may have made an error in citing Alfonta *et al.* Applicants point out that the present utility application claims priority to Prov. Appl. Serial No. 60/511,532, which has a filing date of October 14, 2003. Thus, Alfonta *et al.* is not prior art. The claimed invention is fully supported by the provisional application that was filed prior to the publication of Alfonta *et al.* Applicants assert that Alfonta *et al.* is not prior art, and respectfully request its removal from consideration.

The Claims Require a Plurality of Redox Active Amino Acids

In the Office Action, claims 31 and 33-44 were rejected under 35 U.S.C. §102(e) as allegedly anticipated by Schultz *et al.*, U.S. Patent No. 7,045,337.

As an initial matter, to clarify the record in light of statements in the Action, Applicants point out that U.S. Patent No. 7,045,337 and the subject application do not have the same assignee. 7,045,337 is assigned to The Scripps Research Institute and also to The Regents of the University of California. The subject application is solely assigned to The Scripps Research Institute.

In the rejection over the '337 patent, the Examiner argued that the claims are allegedly anticipated "as evidenced by Rodriguez" (see the Office Action at page 5, last line on the page). It is unclear whether an anticipation or obviousness rejection is intended. In a separate basis for rejection, the Examiner rejected claims 31, 33 and 39-44 under 35 U.S.C. §102(b) as allegedly anticipated by Rodriguez *et al.*, "The Reciprocal Exclusion by L-DOPA

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(3,4-hydroxy-L-phenylalanine) and L-Tyrosine of the Incorporation as Single Units into a Soluble Rat Brain Protein," *Biochemistry Journal* 149:115-121 (1975).

Applicants respectfully traverse these rejections, to the extent that they are applied to the amended claims. Solely for the purpose of advancing the prosecution, and without acquiescing to the rejection, Applicants have amended claim 31. Rebuttal to the rejections is made in view of the amended form of claim 31.

The amended version of independent claim 31 now requires that a protein of the invention comprise *two or more* redox active amino acids. This limitation was previously recited in dependent claim 37, which is now cancelled and incorporated into claim 31. Amendments to dependent claims 35, 36, 38 and 43 revised the language to reflect proper antecedent basis consistent with the amended independent claim 31. The amendment to claim 35 also clarifies that the protein can comprise additional unnatural amino acids that are not redox active amino acids (see paragraphs 0059, 0089, 0118 and 0168).

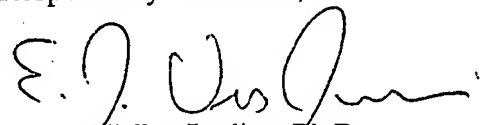
In order for a reference to anticipate a claim, or for a combination of references to render the claim obvious, the reference(s) must teach each and every element of the claim. The Examiner has not established how the prior art teaches a protein with two or more 3,4-dihydroxy-L-phenylalanine (DHP), 3,4,5-trihydroxy-L-phenylalanine, 3-nitro-tyrosine, 4-nitro-phenylalanine, or 3-thiol-tyrosine, or how the prior art provides the additional features of the dependent claims. Accordingly, a prima facie case has not been made and Applicants respectfully request that these rejections be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe that all claims now pending in this application are definite, novel and non-obvious, and are in condition for allowance. The issuance of a formal Notice of Allowance is respectfully requested.

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Respectfully submitted,


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Appl. No. 10/575,991

Response to Office Action dated March 26, 2007

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Attachments:

- 1) a transmittal sheet;
- 2) a fee transmittal sheet;
- 3) petition for three months extension; and
- 4) a receipt acknowledgement postcard.